REMARKS

Upon entry of this amendment, claims 1, 69, and 71-77 will pending. Claims 9, 59, 62, and 68 are canceled without prejudice or disclaimer. Claims 1, 69, 71, and 71-72 have been amended. Claims 73-77 have been added. Support for the amendments is found throughout the specification of application 08/870,608, as originally filed, and the amendments thus do not introduce new matter.

Claim 1 has been amended to more clearly describe the claimed invention. Support for claim 1 as amended may be found throughout the specification, for example at pages 11, lines 3-24; page 13, line 31 to page 14, line 6; and at Examples 27 and 28 at pages 92-101. Claim 69 has been amended for consistency and to more clearly describe the claimed invention. Support for claim 69 as amended may be found throughout the specification, for example at page 24, line 10-13. Claims 71 and 72 have been amended for consistency and to more clearly describe the claimed invention. Support for claims 71 and 72 as amended may be found throughout the specification, for example at page 8, lines 22-29 and page 24, line 20-33. Claims 73-77 have been added. Support for claim 73 can be found, for example at page 11, lines 3-13, page 13 line 19 to page 14, line 12; and original claims 49-53. Support for claim 74 can be found, for example at page 24, lines 10-13. Support for claim 75 can be found, for example at page 27, lines 5-8; and at Table 1 of Example 27-a at page 93. Support for claim 76 can be found for example, at pages 11, lines 3-24; page 13, line 19 to page 14, line 12; and at Examples 27 and 28 at pages 92-101. Support for claim 77 can be found, for example at page 11, lines 3-13, page 13 line 19 to page 14, line 12. Thus, the claims are fully supported by the application as filed and the amendments add no new matter.

Priority

Benefit of priority to application 08/870,608 was denied for claim 62. See Office Action mailed July 25, 2007 (Office Action) at page 3. Without acquiescing to the rejection of priority and solely to advance prosecution, claim 62 has been cancelled without prejudice or disclaimer. Thus, the rejection of priority for that claim is moot.

Double Patenting

Claims 1, 9, 59, and 68-72 were provisionally rejected as allegedly "unpatentable over claims 1, 5, 8, 19-22, 54, 57, and 63 of copending Application No. 10/700697." Office Action at page 4. Claims 1, 9, 59, and 68-72 were also provisionally rejected as allegedly "unpatentable over claims 1, 7-9, 16, 18-22, 26-31, 73, and 76-85 of copending Application No. 10/701,264." Office Action at page 5. Claims 1, 9, 59, and 68-72 were also provisionally rejected as allegedly "unpatentable over claims 1, 5, 9, 11, 75, 78, and 93-97 of copending Application No. 10/701,316." Office Action at page 6. Applicants respectfully request that these provisional rejections based on obvious type double patenting be held in abeyance until claims are found otherwise allowable.

Rejection under 35 U.S.C. § 112

Claim 1 was rejected under 35 U.S.C. § 112, second paragraph as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention." Office Action at page 7. Specifically, claim 1 was rejected as allegedly indefinite "because it recites an oligomeric compound that is only required to be about 12 nucleotides in length that nevertheless must have at least 17 nucleobases complementary to a target nucleic acid." Id. Without acquiescing to the rejection, claim 1 has been amended. Claim 1 as amended does not recite "17 nucleobases." Thus, the rejection is moot. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112.

Rejection Under 35 U.S.C. § 102

Claims 1, 9, 59, and 68-70 were rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Bevilacqua et al., Biochemistry, 1996 (Bevilacqua). See Office Action at page 7. Without acquiescing to the rejection and solely to advance prosecution, claim 1 has been amended. As amended, claim 1 recites a first chemically synthesized oligomeric compound that is "100% complementary to . . . a selected target mRNA." Since the modified sequence in Bevilacqua is not 100% complementary to a target mRNA, Bevliacqua does not anticipate claim 1.

The Examiner asserts that "Bevilacqua et al. disclose (see figure 5 and description on page 9988, first column) chimeric dsRNA duplexes that correspond to the 22 nucleotides of the TAR gene." Office Action at page 8. Applicants respectfully disagree. First, Applicants note that TAR is not a "target mRNA" as recited in the present claims, nor is it a "gene" as suggested by the Examiner, but rather it is an untranslated regulatory sequence of HIV RNA. See e.g., Gunnery et al., Proc. Natl. Acad. Sci., 87:8687-8691 (1990)(copy enclosed). Thus, even if Bevilacqua taught chemically synthesized oligomeric compounds 100% complementary to TAR, Bevilacqua would not anticipate the present claims.

Moreover, on close inspection, it is clear that the modified duplexes discussed in Figure 5 and on page 9988 are not even complementary to TAR. Bevilacqua does discuss experiments conducted with TAR RNA (e.g., pages 9986-9987 and Figures 1-3), however, the RNA used in those experiments was unmodifed. Bevilacqua then describes experiments designed to assess the "sequence independent recognition by a protein." Page 9991, second col. (discussing the experiments described on page 9988 and in Figures 4 and 5). Those experiments used modified oligomeric compounds, but did not use the TAR sequences. Indeed, Bevilacqua contrasts findings from these experiments with those "observed in TAR and dsTAR experiments." Id. Though it is not clearly identified in Bevilacqua, the sequence used in the experiments of Figure 5 appear to be random variants of TAR, as the two sequences are similar.

Thus, the modified oligomeric duplex discussed in Bevilacqua at Figure 5 appears to comprise a deliberately mismatched variant of an untranslated regulatory sequence. As such, it clearly cannot anticipate claim 1, which recites a duplex wherein one strand is 100% complementary to a target mRNA. For at least that reason, Applicants respectfully submit that claim 1 is not anticipated by Bevilacqua. Claims 9, 59, and 68, have been canceled rendering the rejection moot as to those claims. Claims 69, 70, and new claims 73-76 depend from claim 1 thus, those claims are not anticipated by Bevilacqua. Applicants respectfully request that the rejection under § 102 based on Bevilacqua be withdrawn.

Claims 1, 9, 59, and 68-70 were rejected under § 102 as allegedly anticipated by Yu et al., RNA, 1997 (Yu). Without acquiescing to the rejection and solely to advance prosecution, claim 1 has been amended. As amended, claim 1 recites a first chemically synthesized oligomeric

compound that is "100% complementary to . . . a selected target mRNA." Since the modified sequence in Yu is not 100% complementary to a target mRNA, Yu does not anticipate claim 1. As noted by the Examiner, the modified duplexes in Yu correspond to a portion of 28S ribosomal RNA. Therefore, Yu does not disclose every element of claim 1.

For at least that reason, Applicants respectfully submit that claim 1 is not anticipated by Yu. Claims 9, 59, and 68, have been canceled rendering the rejection moot as to those claims. Claims 69, 70, and new claims 73-76 all ultimately depend from claim 1 thus, those claims are not anticipated by Yu. Applicants respectfully request that the rejection under § 102 based on Yu be withdrawn.

Claim 62 was rejected as allegedly anticipated by Brown et al., US 2004/0029257. Solely to advance prosecution and without acquiescing to the rejection, claim 62 has been cancelled without prejudice or disclaimer. Accordingly, the rejection is moot.

Applicants respectfully request withdrawal of all rejections under 35 U.S.C. § 102.

Rejection Under 35 U.S.C. § 103

Claims 1, 9, 59, and 68-72 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Biegleman et al., Journal of Biological Chemistry, 1995 (Beigleman) in view of Koizumi et al.,(Nucleic Acids Research, 1989 (Koizumi) and Stec et al., US 5,151,510 (Stec). Applicants respectfully traverse.

As the Examiner correctly notes, Beigleman is directed to hammerhead ribozymes. See Office Action at page 11. When bound to an RNA substrate, the hammerhead ribozymes described by Beigleman all have at least one region of self-complementarity (stem) and a loop or bulge structure. See e.g., Figure 1. Consequently, such ribozymes are not "100% complementary to said second chemically synthesized oligomeric compound and to a selected target mRNA" as recited in claim 1.

The Examiner cites Koizumi to show "a hammerhead ribozyme substrate sequence that is about 12 to 30 nucleotides in length that is as least partially complementary to a hammerhead ribozyme and comprises a plurality of ribose nucleotides and at least one 2'-OCH3 substituted

nucleotide." Office Action at page 12. Since this reference also discusses hammerhead ribozymes comprising stem and loop structures, none of the disclosed duplexes comprise a first oligomeric compound that is 100% complementary to a second oligomeric compound and to a selected target mRNA as recited in claim 1.

The Examiner cites Stec for its dicussion of phosphorothioate linkages. See Office Action at page 12. Stec does not remedy the deficiencies of Biegleman regarding complementarity.

For at least that reason, Claim 1 is not obvious in view of Beigleman, Koizumi and Stec. The remaining claims all ultimately depend from claim 1 and thus are likewise non-obvious. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103 based on Beigleman in view of Koizumi and Stec.

Claims 1, 9, 59, and 68-72 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Yu in view of Stec. Applicants respectfully traverse. As noted above, the oligonucleotides discussed in Yu comprise a sequence of ribosomal RNA and not mRNA as recited in claim 1. The Examiner cited Stec as an example of modified linkages, such as phophoroathioate linkages to support the rejection of claims 71 and 72. See Office Action at page 13. Thus Stec does not remedy the deficiency of Yu: that it is not directed to mRNA sequences as currently claimed. For at least that reason, Yu does not render the present claims obvious.

Moreover, the Examiner offers no reason why one of skill in the art would combine the teachings of Yu and Stec. Yu discusses a single duplex in which both strands comprise at least one modified nucleoside. See Figure 1C duplex on right. In Figure 1C, Yu first shows successful RNase H cleavage of a substrate RNA that is hybridized with a modified antisense oligonucleotide (duplex on left) and then demonstrates that a single modified nucleoside in the substrate strand destroyed RNase H cleavage (duplex on right). The Examiner has not provided any reason why one of ordinary skill in the art would incorporate phosphorothioate linkage into such duplexes. Although the Examiner notes that phosphorothioate linkages "provide the advantages of increased stability and nuclease resistance," the Examiner has not provided any reason why one of skill in the art would be motivated to further modify the duplex on the right of

Figure 1C of Yu to enhance stability or nuclease resistance. Indeed, Yu suggests that such further modification will result in more duplexes incapable of supporting RNase H activity. Absent such reason, the combination of Yu and Stec would not render obvious claims 71 and 72, even if Yu were not limited to ribosomal RNA.

Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103 based on Beigleman in view of Yu and Stec.

Applicants respectfully request withdrawal of all rejections under 35 U.S.C. § 103.

Conclusion

Applicants respectfully submit that the present application is in condition for allowance. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Favorable consideration and a notice of allowance are respectfully requested.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 50-0252.

Respectfully submitted,

Date: **January 25, 2008**

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